REMARKS

I. STATUS OF THE APPLICATION

Claims 1, 6-9, 11-15, 17-18, 22-28 and 43-53 are presently pending. Claims 1, 6, 7, 9, 22, 43-45, 47, 48 and 50-53 stand rejected, and claims 8, 11-15, 17-18, 22-28, 46 and 49 have been objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

II. CLAIMS 1, 6-7, 9 AND 22 ARE PATENTABLY DISTINCT OVER CO-PENDING APPLICATION NO. 10/531,526

Claims 1, 6-7, 9 and 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-30, 39-45 and 47-48 of co-pending Application No. 10/531,526 (the "'526 Application). Applicants respectfully traverse this rejection.

Claims 1, 6-7, 9 and 22 of the present application are patently distinct from claims 27-30, 39-45 and 47-48 of the '526 Application because the two pending applications claim different methods with different limitations administered to different subject populations. Claim 1 of the present application teaches, among other things, a method of treating or reducing the risk of developing a depressive disorder in a subject in need thereof, comprising providing and administering a therapeutically effective amount of a composition that comprises testosterone, isopropyl myristate, a thickening agent, lower alcohol and water. The claimed invention also teaches a defined pharmacokinetic profile. In particular, after administration of a therapeutically effective amount of the composition, the serum concentration is substantially maintained between about 400 ng testosterone per dL to about 1050 ng testosterone per dL.

On the other hand, the '526 Application claims a method of improving sexual performance in a male or animal subject, comprising administering a pharmaceutical composition that comprises testosterone, isopropyl myristate, alcohol, a gelling agent, and administering a pharmaceutical agent for treating erectile dysfunction.

The instant invention is directed to both male and female subjects, while the '526 Application is directed only to male subjects. In addition, as the Examiner admits, the instant invention teaches a method of treating depressive disorder, while the '526 Application teaches a method of improving sexual performance. The Examiner provides no evidence for its allegation that "patients with erectile dysfunction may necessarily be depressed." Office Action at 4-5. Applicants contend that a method of treating or reducing the risk of developing a depressive disorder is patentably distinct from a method for improving sexual performance in a male. Indeed, the '526 Application requires the administration of a pharmaceutical agent for treating erectile dysfunction to the male subject in order to improve sexual performance of the subject. The present application does not teach use of a pharmaceutical agent for treating erectile dysfunction. Further, the '526 Application does not claim the pharmacokinetic profiles claimed in the present invention, nor the specific amounts of the ingredients of the claimed pharmaceutical composition.

For the foregoing reasons, Applicants respectfully submit that claims 1, 6-7, 9 and 22 are not obvious over claims 27-30, 39-45 and 47-48 of the '526 Application. Accordingly, Applicants request withdrawal of the provisional nonstatutory obviousness-type double patenting rejection of claims 1, 6-7, 9 and 22.

III. CLAIMS 1, 6-7, 9 AND 22 ARE PATENTABLY DISTINCT OVER CO-PENDING APPLICATION NO. 10/867,435

Claims 1, 6-7, 9 and 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-30, 39-45 and 47-48 of co-pending Application No. 10/867,435 (the "'435 Application). Applicants respectfully traverse this rejection.

Claims 1, 6-7, 9 and 22 of the present application are patently distinct from claims 27-30, 39-45 and 47-48 of the '435 Application because the two pending applications claim different methods with different limitations administered to different subject populations. Claim 1 of the present application teaches, among other things, a method of treating or reducing the risk of developing a depressive disorder in a subject in need thereof, comprising providing and administering a therapeutically effective amount of a composition that comprises testosterone, isopropyl myristate, a thickening agent, lower alcohol and water. The claimed invention also

teaches a defined pharmacokinetic profile. In particular, after administration of a therapeutically effective amount of the composition, the serum concentration is substantially maintained between about 400 ng testosterone per dL to about 1050 ng testosterone per dL.

On the other hand, the '435 Application claims a method of improving of improving sexual performance in a male or animal subject, comprising administering a pharmaceutical composition comprising testosterone, a penetration enhancer, alcohol, a gelling agent, and administering a pharmaceutical agent for treating erectile dysfunction.

The instant invention is directed to both male and female subjects, while the '435 Application is directed only to male or animal subjects. In addition, as the Examiner admits, the instant invention teaches a method of treating depressive disorder, whereas the '435 Application teaches a method of improving sexual performance. The Examiner provides no evidence for its allegation that "patients with erectile dysfunction may necessarily be depressed." Office Action at 6. Applicants contend that a method of treating or reducing the risk of developing a depressive disorder is patentably distinct from a method for improving sexual performance in a male. Indeed, the '435 Application requires the administration of a pharmaceutical agent for treating erectile dysfunction to the male subject in order to improve sexual performance of the male subject. The present application does not teach use of a pharmaceutical agent for treating erectile dysfunction. Further, the '435 Application does not claim the pharmacokinetic profiles claimed in the present invention, nor the specific amounts of the ingredients of the claimed pharmaceutical composition.

For the foregoing reasons, Applicants respectfully submit that claims 1, 6-7, 9 and 22 are not obvious over claims 27-30, 39-45 and 47-48 of the '435 Application. Accordingly, Applicants request withdrawal of the provisional nonstatutory obviousness-type double patenting rejection of claims 1, 6-7, 9 and 22.

IV. CLAIMS 43-45, 47-48 AND 50-53 ARE PATENTABLY DISTINCT OVER CO-PENDING APPLICATION NO. 10/867,445

Claims 43-45, 47-48 and 50-53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 33, 39-41, 44, 57, 68, 70-

72 and 74-75 of co-pending Application No. 10/867,445 (the "'445 Application"). Applicants respectfully traverse this rejection.

Claims 43-45, 47-48 and 50-53 of the present application are patently distinct from the composition of claims 33, 39-41, 44, 57, 68, 70-72 and 74-75 of the '445 Application. Claim 43 of the present application teaches, among other things, a method of transdermally delivering a hydroalcoholic gel composition to a male subject in need thereof resulting in the stated pharmacokinetic profile wherein the hydroalcoholic gel composition consists essentially of testosterone, an alcohol, isostearic acid, a thickening agent and water in amounts set forth therein. On the other hand, the '445 Application teaches a method of treating hypogonadism in a male subject in need thereof, comprising administering a hydroalcoholic gel pharmaceutical composition that comprises testosterone, alcohol, a penetration enhancer consisting essentially of isopropyl myristate, a gelling agent and water. Notably, claims 33, 39-41, 44, 57, 68, 70-72 and 74-75 of the '445 Application fail to teach isostearic acid as a penetration enhancer.

In addition, neither of the references teach that isostearic acid and isopropyl myristate are functionally equivalent as penetration enhancers and substitutable. Indeed, the Examiner has failed to identify any reason why a person of ordinary skill in the art at the time of invention would have combined the cited references to obtain the claimed invention. Specifically, Applicants contend that the '445 Application provides no motivation to substitute its claimed penetration enhancer with isostearic acid. To be sure, the Food and Drug Administration (FDA), a sister agency, has recognized that penetration enhancers used for transdermal delivery of testosterone are not simplistically substitutable. *Auxilium Pharmaceutical, Inc. Citizen's Petition Decision*, August 26, 2009, Docket No. FDA-2009-P-0123 (copy provided in the June 1, 2010 Information Disclosure Statement).

In particular, in the context of transdermal testosterone gels, the FDA has found that any change in the penetration enhancer creates an unknown risk of testosterone transfer. Thus, the FDA has precluded the approval of a generic transdermal testosterone via an Abbreviated New Drug Application and now requires a full New Drug Application to be filed so that any alterations in the transfer of testosterone to persons in contact with the patient using the testosterone gel can be fully studied and understood. *Id.* at 5. The FDA also recognized what is replete in the literature: that different penetration enhancers may affect skin differently and may

cause different degrees of skin irritation and sensitization. *Id.* at 7. Accordingly, the effect of different penetration enhancers in transdermal testosterone gels is unpredictable and cannot be presumed an obvious substitution.

In addition, the FDA decision provides evidence that a person of ordinary skill in the art would not have a reasonable expectation of success when simply substituting penetration enhancers in transdermal formulations, especially transdermal formulations containing testosterone. Therefore, one of skill in the art would have no reasonable expectation of success that the penetration enhancer–isostearic acid–could be substituted in the claimed invention.

For the foregoing reasons, Applicants respectfully submit that claims 43-45, 47-48 and 50-53 are not obvious over claims 33, 39-41, 44, 57, 68, 70-72 and 74-75 of the '445 Application. Accordingly, Applicants request withdrawal of the provisional nonstatutory obviousness-type double patenting rejection of claims 43-45, 47-48 and 50-53.

CONCLUSION

For at least the foregoing reasons, it is respectfully submitted that the pending claims are in condition for allowance. Early and favorable consideration is respectfully requested, and the Examiner is encouraged to contact the undersigned with any questions or to otherwise expedite prosecution. Further, none of Applicants' amendments are to be construed as dedicating any such subject matter to the public, and Applicants reserve all rights to pursue any such subject matter in this or a related patent application.

Kindly contact the undersigned with any questions or to otherwise expedite prosecution.

Respectfully submitted,

/s/ Joseph A. Mahoney
Joseph A. Mahoney
Reg. No. 38,956

CUSTOMER NUMBER 26565
MAYER BROWN LLP
P.O. Box 2828
Chicago, IL 60690-2828

Telephone: (312) 701-8286
Facsimile: (312) 706-9000